West Nile Virus – General, Surveillance, and Laboratory Information

General Information on West Nile Virus (WNV)

WNV is a flavivirus in the same family as St. Louis encephalitis (SLE) virus. WNV and SLE-virus are very closely related and, in fact, the ELISA antibody test for SLE cross-reacts with West Nile. Both viruses can cause encephalitis, aseptic meningitis, and mild febrile illness, but the vast majority of infected persons will be asymptomatic.

The epidemiology and clinical presentation of WNV are similar to SLE; transmission occurs through the bite of an infected mosquito. Wild birds appear to be the main reservoir of the virus; however, the virus has also been found, but is far less common, in chickens, horses, and other mammals. ***The infection cannot be transmitted from birds or other animals to humans or from person to person, but is spread by mosquitoes that have bitten birds or other animals carrying the virus. Mosquitoes can then transmit the infection to humans through a mosquito bite.***

Similar to SLE, the primary mosquito vectors for WNV are *Culex* species, *Anopheline* species, and *Aedes vexans* which are mosquitoes that are known to be in the New River Valley. Unlike *Culex* and *Anopheline* species, *Aedes vexans* can bite during the day so that persons need to be cautioned to use mosquito precautions during the day, as well as in the evening hours when the other species are active.

The symptoms of WNV are similar to those of SLE virus. The incubation period for WNV is thought to vary from 5 to 15 days. Most people who are infected are asymptomatic or may experience milder illnesses, with fever and headache, before fully recovering. Rash, conjunctivitis, lymphadenopathy, hepatitis, and pancreatitis have also been reported. In the elderly, WNV can cause more serious neurologic disease and can be fatal.

Surveillance Criteria for Human Encephalitis and Meningitis

During the 1999 outbreak in New York, two-thirds of the encephalitis cases were associated with severe muscle weakness. Documentation of muscle weakness was based on neurologic examination and/or electromyogram (EMG) findings. Therefore, case ascertainment should include encephalitis with muscle weakness, which may be more likely to represent WNV than other viral causes of encephalitis.

It should be noted that the background rate of viral (aseptic) meningitis is significantly higher than encephalitis, and mostly due to enteroviruses, such as Echo and Coxsackie, during the summer and fall months, especially in young children. Therefore, the Virginia Department of Health does NOT intend to include viral meningitis in the surveillance criteria for Virginia unless there is evidence of WNV activity in Virginia or more resources are available. Although the increase in caseload may improve case detection, it will generate significantly more testing requests and reagents are limited.

1. **Recommended Criteria for Suspect Case of WNV** - Any adult or pediatric patient with viral encephalitis (Criteria a, b and c below) with or without associated muscle weakness (Criteria d)

1. Fever $\geq$ 38ºC or 100ºF, and
2. Altered mental status (altered level of consciousness, agitation, lethargy) and/or other evidence of cortical involvement (e.g., focal neurologic findings, seizures), and
3. CSF pleocytosis with predominant lymphocytes and/or elevated protein and a negative gram stain and culture, and/or
4. Muscle weakness (especially flaccid paralysis) confirmed by neurologic exam or by EMG

2. **Laboratory Testing for WNV**

Any adult or pediatric patient admitted to a hospital with a presumed diagnosis of viral encephalitis, or with focal CNS findings and fever, and who fits the above "Recommended Criteria for Suspect Case of WNV" should have whole blood or serum submitted for diagnostic testing at our State laboratory, the Division of Consolidated Laboratory Services (DCLS).

Certainly, all suspect cases should be reported to either Katherine McCombs, District Epidemiologist, or Dr. Jody Hershey, Director, at the Montgomery County Health Department (540-381-7100, ext. 189 and 156 respectively) using the Epi-1 reporting form, the *Encephalitis/Initial Case Report Form*, or over the telephone. Arboviral encephalitis is one of more than 70 reportable disease and conditions in Virginia.

Because of limited capacity, ONLY those patients who meet the recommended criteria for encephalitis will be tested through DCLS. Patients with milder illnesses (e.g., fever and headache, fever and rash, fever and lymphadenopathy) or no symptoms (e.g. persons

with a recent mosquito bite but no acute symptoms) do not need to be tested for WNV—see section *3. Managing Patients with Milder Illness.*

Testing by commercial laboratories is discouraged based on past experiences with unreliable results--especially since WNV may cross-react with SLE on commercially available serologic tests. DCLS performs highly specific IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) and IgG ELISA on sera and CSF to identify St. Louis encephalitis (SLE), Eastern Equine encephalitis (EEE), Lacrosse encephalitis (LAC), and WNV-reactive antibody. Additionally, they perform RT-PCR on post morten tissue or CSF. Reactive specimens are then immediately forwarded to the Centers for Disease Control and Prevention (CDC) for confirmation with a plaque reduction neutralization test (PRNT).

Appropriate specimens for testing include:

- Sera – Appropriately timed acute and convalescent sera for testing by MAC-ELISA and IgG ELISA.
- CSF - Testing by MAC-ELISA, real-time RT-PCR, or viral isolation.
- IgM-positive sera should be confirmed by convalescent sera (IgG ELISA and PRNT).
- Brain tissue – Real-time RT-PCR and viral isolation.

Physicians and laboratories are encouraged to complete all essential information on the laboratory submission forms. Accurate interpretation of serological findings requires knowledge of the specimen. For human specimens, it is important that the following data accompany specimens submitted for serology before testing can proceed or results can be properly interpreted and reported:

- symptom onset date, when known
- date of sample collection
- unusual immunological status of patient (immunosuppression)
- current address and travel history in flavivirus-endemic area
- history of prior vaccination against flavivirus disease (Yellow fever, Japanese Encephalitis, or Central European Encephalitis)
- brief clinical summary including suspected diagnosis (encephalitis or aseptic meningitis).

Patient information and laboratory data will be shared between the Virginia Department of Health and local health departments (LHDs) on a secure e-mail system to facilitate case surveillance and timely reporting of laboratory results back to the LHDs.

In the event that acute specimens (obtained within 10 days of illness onset)

are negative by ELISA testing, laboratory diagnosis of WNV will require that a follow-up (convalescent) blood sample be obtained at least 2 weeks after the acute specimen to evaluate for the presence of convalescent antibody to the virus.

The laboratory summary sheet, *Division of Consolidated Laboratory Services (DCLS) Arbovirus Testing*, summarizes testing criteria, types and amounts of specimens to be submitted, and packaging and shipping.

3. **Managing Patients with Milder Illness**

Many asymptomatic patients who report mosquito bites, or patients who have mild symptoms--such as fever, headache, lymphadenopathy, and/or a rash---may present to medical facilities over the coming weeks and request specific testing for WNV. In areas where transmission of the WNV is known to be occurring, only a small portion of mosquitoes (~1/1000) are likely to be infected with WNV. If a person is bitten by an infected mosquito, the chance of developing illness is approximately 1/300. Finally, enteroviruses capable of causing symptoms and mild illnesses similar to WNV are also known to be circulating widely in August and September. **Most patients with mild symptoms will NOT have WNV, and DO NOT require specific diagnostic testing for WNV.**

Patients should be reassured and told that:

- They are unlikely to have WNV;
- Patients with mild symptoms will likely recover completely, and do not require any specific medication;
- Laboratory testing for WNV is not necessary for patients with mild symptoms; and
- They should seek medical attention if they develop more severe symptoms such as confusion, lethargy, muscle weakness, severe headache, stiff neck, or photophobia.

Encephalitis / Initial Case Report Form

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